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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/737,476	12/18/2000	Leo G.J. Frenken	P 0275850 T 7060C	9341

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	**PAPER NUMBER**
1638	

DATE MAILED: 11/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/737,476	FRENKEN ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 16* is/are pending in the application.

4a) Of the above claim(s) *8 and 10-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 29, 2006 has been entered.

Claims 14-15 are cancelled.

Claims 1 and 16 are currently amended.

Claims 8 and 10-13 are withdrawn.

Claims 1-13 and 16 are pending.

Claims 1-7, 9 and 16 are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 103

Claims 1-4, 6-7 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of Magnuson et al. (Enhanced recovery of a secreted mammalian protein from suspension culture of genetically modified tobacco cells. Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. I (WO 94/04678, 3 March 1994, Applicant's IDS) or Casterman et al. II (US Patent No. 5,759,808, issued June 2, 1998), in view of Owen et al. (Synthesis of a

functional anti-phytochrome single-chain Fv protein in transgenic tobacco. Biotechnology, Vol. 10, pages 790-794, July 1992), Moloney M.M. et al. (Subcellular targeting and purification of recombinant proteins in plant production systems. Biotechnol Genet Eng Rev. 1997;14:321-36. Review), Herrera-Estrella L. et al. (US Patent No. 5,728,925, issued March 17, 1998) and Hilton J.R. (An association of phytochrome with the chloroplast envelope membranes of *Spinacia oleracea* L.: a preliminary observation. New Phytol., 1983, Vol. 95, pages 175-178).

The claims are drawn to method for producing a functional heavy chain antibody or an active fragment of heavy chain antibody showing the antigen binding activity of the antibody in a plant, comprising introducing into said plant a DNA sequence which encodes an antibody that is a heavy chain immunoglobulin devoid of a variable light chain domain, or an active fragment of said immunoglobulin devoid of a variable light chain domain, wherein antigen-binding capacity is located in a single binding domain, and expressing said antibody or said active fragment, said DNA sequence also including a sequence which expresses a peptide which targets said antibody or fragment thereof to the plastid of said plant, including methods wherein the heavy chain immunoglobulin or fragment thereof is obtainable from camelids, methods wherein the plant is selected from tobacco, pea, potato, spinach, tomato or tea, methods wherein the heavy chain immunoglobulin or active fragment thereof binds to a protein present in the plant, methods wherein the heavy chain immunoglobulin or active fragment thereof binds to a plant hormone or plant metabolite, and methods wherein the plastid is a chloroplast. The claims are also drawn to a plant prepared according to the method of claim 1, and seeds, fruits, progeny and hybrids of the plant according to claim 7 which comprise a DNA sequence encoding a heavy chain immunoglobulin or active fragment thereof.

Magnuson et al. teach a method for modifying a plant to produce an antibody comprising introducing into tobacco suspension culture cells a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain and obtained from a 93G7 monoclonal antibody, said sequence being operably linked to a CaMV 35S promoter, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen, in the cytoplasm and plasma membrane (page 222 Figure 1; page 223 Table 1 and Figures 2-3; page 224 Figures 4-5; page 225 Table 2; page 226 Figure 9).

Casterman I. et al. teach a method for modifying a plant to produce an antibody by introducing into a plant a DNA sequence encoding a heavy chain immunoglobulin obtainable from camelids (page 33 first paragraph).

Casterman II. et al. teach a method for producing camelid antibodies in a plant by introducing into a plant a DNA sequence encoding a camelid antibody (column 15 lines 42-47; column 16 lines 12-18; column 17 lines 64-67; column 18 lines 52-60; column 112 claim 8). The heavy chain immunoglobulins obtainable from camelids are heavy chain only antibodies, devoid of a variable light chain domain, with their antigen binding capacity residing in a single binding domain.

Owen et al. teach a method for modifying the response of a plant to light by introducing into a tobacco plant a DNA sequence encoding an antigen-binding single chain F_v protein (scF_v), said scFv comprising the heavy and light chain variable domain coding regions from a mouse monoclonal IgG1 anti-phytochrome antibody (page 790 Figure 1; page 791 column 2 second full paragraph and Figure 2; page 792 Figure 4; page 794 column 1 second full paragraph). The DNA sequence encoding the antigen-binding scFv protein taught by Owen et al. encodes a heavy chain

immunoglobulin or an active fragment or derivative thereof (page 790 Figure 1; page 791 Figure 2) that binds to a phytochrome protein present in the plant (page 792 Table 1; page 793 Figure 5). The phytochrome protein is also a plant hormone because phytochrome regulates plant growth responses to light. The phytochrome protein is additionally a plant metabolite because phytochrome is a product of plant metabolism.

Magnuson et al., Casterman et al. I, Casterman et al. II and Owen et al. do not teach a DNA sequence also including a sequence which expresses a peptide which targets said antibody or fragment thereof to the plastid of said plant.

Moloney M.M. et al. teach the targeting of recombinant proteins to the chloroplast as a means to alter genetic and biochemical functions within the chloroplast (pages 328-330).

Herrera-Estrella L. et al. teach a DNA sequence also including a sequence which expresses a peptide which targets a heterologous protein to a plant chloroplast (figures 1, 3, 8, 14; column 1 lines 16-18; columns 33-38). Herrera-Estrella L. et al. also teach that the heterologous protein may consist of any protein or peptide sought to be introduced into the chloroplasts of determined plants (column 9 lines 34-43).

Hilton J.R. teaches localization of phytochrome in plastids and chloroplasts (introduction; page 177).

Given the success of Magnuson et al. in expressing in a plant cell a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of specific binding with an antigen or the teaching of Casterman et al. I and II to do the same in a plant, given the success of Owen et al. in expressing in a plant a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is

a phytochrome protein present in a plant, given the teachings of Hilton J.R. that some cellular phytochrome is localized in the chloroplast and plastids, given the teachings of Moloney M.M. et al. that recombinant proteins can be targeted to the chloroplast as a means to alter functions within the chloroplast, and given the success of Herrera-Estrella L. et al. in using a DNA sequence which expresses a peptide which targets a heterologous protein to a plant chloroplast, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express in a plant any type of immunoglobulin capable of specific binding with an antigen that is a protein present in a plant chloroplast and/or a plant hormone or plant metabolite present in a plant chloroplast, for the purpose of manipulating physiologic processes that are localized within a plant chloroplast, such as phytochrome responses, without any surprising or unexplained results. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claims 1-5, 7, 9 and claim 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of Magnuson et al. (Enhanced recovery of a secreted mammalian protein from suspension culture of genetically modified tobacco cells. Protein Expression and Purification, 1996, Vol. 7, pages 220-228) or Casterman et al. I (WO 94/04678, 3 March 1994, Applicant's IDS) or Casterman et al. II (US Patent No. 5,759,808, issued June 2, 1998), in view of Le Gall et al. (Engineering of a single-chain variable-fragment (scFv) antibody specific for the stolbur phytoplasma (Mollicute) and its expression in Escherichia coli Applied and Environmental

Microbiology, Vol. 64, No. 11, pages 4566-4572, November 1998), Moloney M.M. et al. (Subcellular targeting and purification of recombinant proteins in plant production systems. Biotechnol Genet Eng Rev. 1997;14:321-36. Review), Herrera-Estrella L. et al. (US Patent No. 5,728,925, issued March 17, 1998) and Rohozinski J. et al. (Do light-induced pH changes within the chloroplast drive turnip yellow mosaic virus assembly? J Gen Virol. 1996 Feb;77 (Pt 2):163-5).

The claims are drawn to method for producing a functional heavy chain antibody or an active fragment of heavy chain antibody showing the antigen binding activity of the antibody in a plant, comprising introducing into said plant a DNA sequence which encodes an antibody that is a heavy chain immunoglobulin devoid of a variable light chain domain, or an active fragment of said immunoglobulin devoid of a variable light chain domain, wherein antigen-binding capacity is located in a single binding domain, and expressing said antibody or said active fragment, said DNA sequence also including a sequence which expresses a peptide which targets said antibody or fragment thereof to the plastid of said plant, including methods wherein the heavy chain immunoglobulin or fragment thereof is obtainable from camelids, methods wherein the plant is selected from tobacco, pea, potato, spinach, tomato or tea, methods wherein the heavy chain immunoglobulin or active fragment thereof binds to a protein present in the plant, methods wherein the heavy chain immunoglobulin or active fragment thereof binds to a plant pathogen or animal pathogen, and methods wherein the plastid is a chloroplast. The claims are also drawn to a plant prepared according to the method of claim 1, and seeds, fruits, progeny and hybrids of the plant according to claim 7 which comprise a DNA sequence encoding a heavy chain immunoglobulin or active fragment thereof.

Magnuson et al. teach a method for modifying a plant to produce an antibody comprising introducing into tobacco suspension culture cells a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain and obtained from a 93G7 monoclonal antibody, said sequence being operably linked to a CaMV 35S promoter, and expressing the antibody which is devoid of light chain domains but capable of specific binding with an antigen, in the cytoplasm and plasma membrane (page 222 Figure 1; page 223 Table 1 and Figures 2-3; page 224 Figures 4-5; page 225 Table 2; page 226 Figure 9).

Casterman I. et al. teach a method for modifying a plant to produce an antibody by introducing into a plant a DNA sequence encoding a heavy chain immunoglobulin obtainable from camelids (page 33 first paragraph).

Casterman II. et al. teach a method for producing camelid antibodies in a plant by introducing into a plant a DNA sequence encoding a camelid antibody (column 15 lines 42-47; column 16 lines 12-18; column 17 lines 64-67; column 18 lines 52-60; column 112 claim 8). The heavy chain immunoglobulins obtainable from camelids are heavy chain only antibodies, devoid of a variable light chain domain, with their antigen binding capacity residing in a single binding domain. Casterman et al. II also teach a method for producing camelid antibodies in a plant wherein the camelid antibodies bind to insect gut antigen, said insect being an animal pathogen in that it is a pathogen that is an animal, and a plant pathogen in that it is a pathogen of plants (column 16 lines 12-18).

Le Gall et al. teach a method for modifying a tobacco plant to produce an anti-stolbur phytoplasma antibody by introducing into a tobacco plant a DNA sequence encoding an antigen-binding single chain F_v protein (scF_v), said scFv comprising the heavy and light chain variable

domain coding regions from a monoclonal IgG1 antibody (2A10) directed against the major membrane protein of the stolbur phytoplasma (page 4567 column 2 second full paragraph; page 4568 column 2). The DNA sequence encoding the antigen-binding scFv protein taught by Le Gall et al. encodes a heavy chain immunoglobulin or an active fragment or derivative thereof (page 4567 Figure 1) that binds to stolbur-infected periwinkle extract (page 4569 Table 1). The DNA sequence encoding the antigen-binding scFv protein taught by Le Gall et al. also binds to a protein present in the plant, as transgenic plants are protected against phytoplasma infection, which occurs in the sieve tubes within the phloem (page 4570 Figure 6).

Magnuson et al., Casterman et al. I, Casterman et al. II and Le Gall et al. do not teach a DNA sequence also including a sequence which expresses a peptide which targets said antibody or fragment thereof to the plastid of said plant.

Moloney M.M. et al. teach the targeting of recombinant proteins to the chloroplast as a means to alter genetic and biochemical functions within the chloroplast (pages 328-330).

Herrera-Estrella L. et al. teach a DNA sequence also including a sequence which expresses a peptide which targets a heterologous protein to a plant chloroplast (figures 1, 3, 8, 14; column 1 lines 16-18; columns 33-38). Herrera-Estrella L. et al. also teach that the heterologous protein may consist of any protein or peptide sought to be introduced into the chloroplasts of determined plants (column 9 lines 34-43).

Rohozinski J. et al. teach localization of turnip yellow mosaic virus plant pathogen in chloroplasts.

Given the success of Magnuson et al. in expressing in a plant cell a DNA sequence encoding a heavy chain immunoglobulin devoid of a variable light chain domain but capable of

specific binding with an antigen or the teaching of Casterman et al. I and II to do the same in a plant, and given the success of Le Gall et al. in expressing in a plant a DNA sequence encoding a single-chain Fv recombinant immunoglobulin capable of specific binding with an antigen that is a stolbur phytoplasma plant pathogen, given the teachings of Rohozinski J. et al. that some plant pathogens such as the turnip yellow mosaic virus may be localized in chloroplasts, given the teachings of Moloney M.M. et al. that recombinant proteins can be targeted to the chloroplast as a means to alter functions within the chloroplast, and given the success of Herrera-Estrella L. et al. in using a DNA sequence which expresses a peptide which targets a heterologous protein to a plant chloroplast, it would have been *prima facie* obvious to one skilled in the art at the time the invention was made to express in a plant any type of immunoglobulin capable of specific binding with an antigen that is a protein present in the plant chloroplast and/or a plant pathogen that is localized within a plant chloroplast, for the purpose of improving a plant's resistance to infection by a plant pathogen that is localized within a plant chloroplast, such as turnip yellow mosaic virus, without any surprising or unexplained results. Accordingly, one skilled in the art would have been motivated to generate the claimed invention with a reasonable expectation of success. Thus, the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Double Patenting

Claims 1-7, 9 and 16 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-12 of copending Application No. 11/267,191, filed November 7, 2005, for reasons of record.

Applicants respectfully point out that this is a provisional obviousness-type double patenting rejections between two applications and point to MPEP 804 (I)(B) which indicates that if a provisional double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection. Applicants maintain that MPEP 804 (I)(B) applies given the amendments made to claim 1 addressing the previous rejections under 35 U.S.C. 102(b), 35 U.S.C. 112 (second paragraph) and 35 U.S.C. 103(a).

The rejection is maintained, as the provisional double patenting rejection is not the only rejection remaining.

Claims 1-7, 9 and 16 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-9 and 11-12 of copending Application No. 11/267,310, filed November 7, 2005, for reasons of record.

Applicants respectfully point out that this is a provisional obviousness-type double patenting rejections between two applications and point to MPEP 804 (I)(B) which indicates that if a provisional double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection. Applicants maintain that MPEP 804 (I)(B) applies given the amendments made to claim 1 addressing the previous rejections under 35 U.S.C. 102(b), 35 U.S.C. 112 (second paragraph) and 35 U.S.C. 103(a).

The rejection is maintained, as the provisional double patenting rejection is not the only rejection remaining.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia Collins
Primary Examiner
Art Unit 1638

CC

Cynthia Collins 11/10/06